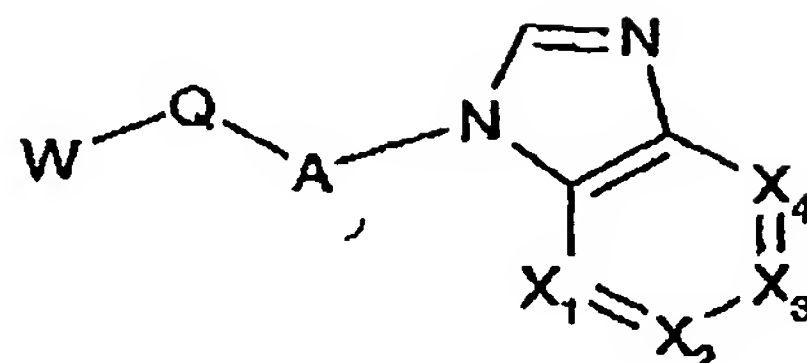


71.

## CLAIMS

1. A compound of the general formula I

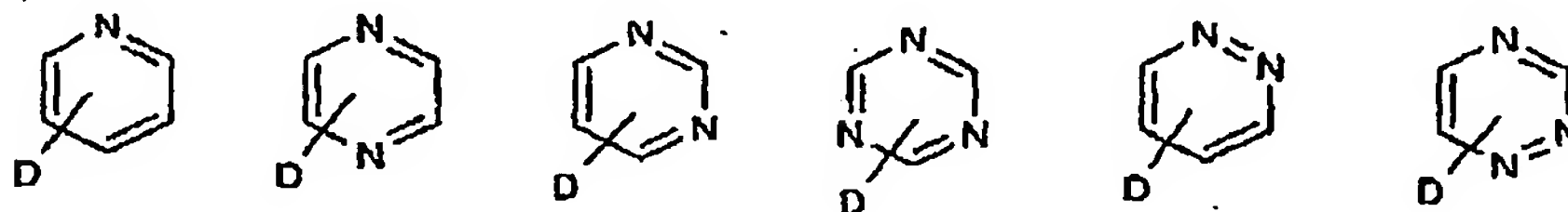


I

- 5 or pharmaceutically acceptable prodrugs, salts, hydrates, solvates, crystal forms or diastereomers thereof, wherein:

$X_1, X_2, X_3, X_4$  are each carbon where one is substituted with Z and the rest independently with Y; or one of  $X_1, X_2, X_3, X_4$  is N, and the others are carbon where one carbon is substituted with Z and the rest independently with Y;

- 10 A is a ring selected from:



where D is selected from H,  $C_{1-4}$  alkyl, halogen, amino;

Q is a bond, halogen,  $C_{1-4}$  alkyl, O, S, SO,  $SO_2$ , CO, CS;

W is:

- 15 (ii)  $NR_1R_2$  where  $R_1$  and  $R_2$  are independently H,  $C_{1-4}$  alkyl,  $C_{1-4}$  alkyl $CP_3$ , aryl, hetaryl,  $C_{1-4}$  alkylaryl,  $C_{1-4}$  alkylhetaryl,  $C_{3-8}$  cycloalkyl,  $C_{2-6}$  alkenyl, cyclohetalkyl,  $C_{1-4}$  alkylcycloalkyl,  $C_{1-4}$  alkyl cyclohetalkyl, or  $R_1$  and  $R_2$  are joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S,  $NR_3$ ; and  $R_3$  is selected from H,  $C_{1-4}$  alkyl, aryl, hetaryl,  $C_{1-4}$  alkyl aryl,  $C_{1-4}$  alkyl hetaryl,  $COR_4$  where  $R_4$  is selected from H,  $C_{1-4}$  alkyl, aryl, hetaryl;
- 20

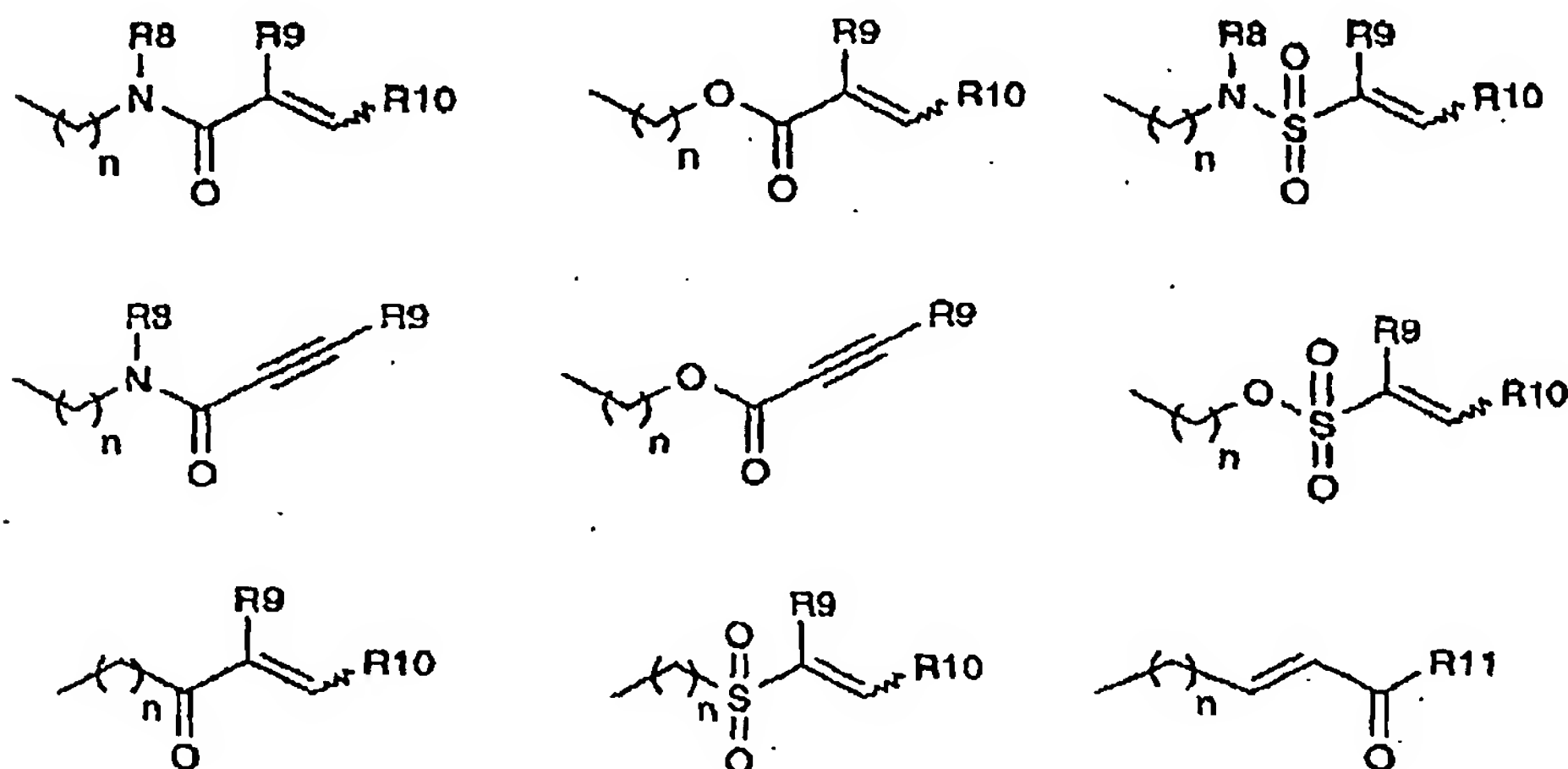
72

OR

(ii) H, C<sub>1-4</sub> alkyl, aryl, hetaryl, C<sub>3-8</sub> cycloalkyl, cyclohetalkyl, C<sub>1-4</sub> alkylaryl, C<sub>1-4</sub> alkylhetaryl, C<sub>3-8</sub> cycloalkyl, C<sub>1-4</sub> alkylcycloalkyl, C<sub>1-4</sub> alkyl cyclohetalkyl;

Y is H, halogen, CN, CF<sub>3</sub>, nitro, OH, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylNR<sub>5</sub>R<sub>6</sub>, C<sub>1-4</sub> alkylhetaryl, OC<sub>1-4</sub> alkyl, OC<sub>2-4</sub> alkylOC<sub>1-4</sub>alkyl, OC<sub>1-4</sub> alkylNR<sub>5</sub>R<sub>6</sub>, OC<sub>1-4</sub> alkylhetaryl, OC<sub>1-4</sub> alkylcyclohetalkyl, SC<sub>1-4</sub> alkyl, SC<sub>2-4</sub> alkylOC<sub>1-4</sub>alkyl, SC<sub>1-4</sub> alkylNR<sub>5</sub>R<sub>6</sub>, NR<sub>5</sub>R<sub>6</sub>, NR<sub>5</sub>COR<sub>6</sub>, NR<sub>5</sub>SO<sub>2</sub>R<sub>6</sub>; and R<sub>5</sub> and R<sub>6</sub> are each independently H, C<sub>1-4</sub> alkyl, or may be joined to form an optionally substituted 3-6 membered ring optionally containing an atom selected from O, S, NR<sub>7</sub> and R<sub>7</sub> is selected from H, C<sub>1-4</sub> alkyl, aryl, hetaryl, C<sub>1-4</sub> alkylaryl, C<sub>1-4</sub> alkylhetaryl;

Z is selected from :



where R<sub>8</sub> is selected from H, C<sub>1-4</sub> alkyl;

R<sub>9</sub> and R<sub>10</sub> are independently selected from H, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylNR<sub>12</sub>R<sub>13</sub>, C<sub>1-4</sub> alkylOR<sub>12</sub>, C<sub>1-4</sub> alkylhetaryl or may be joined to form a 5-8 membered ring optionally containing an atom selected from O, S, SO, SO<sub>2</sub>, NR<sub>14</sub>;

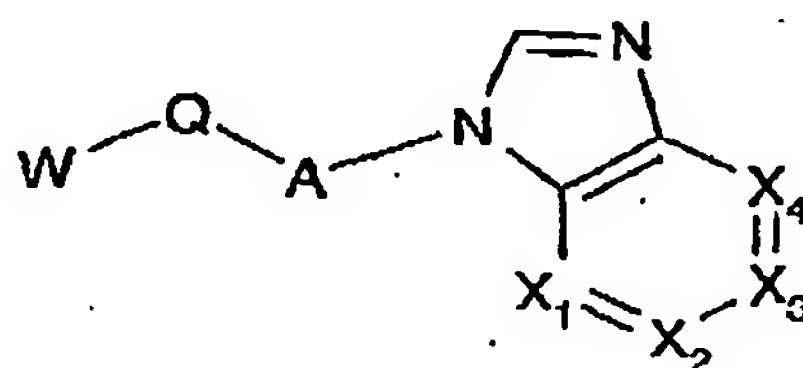
R<sub>11</sub> is selected from OH, OC<sub>1-4</sub> alkyl, NR<sub>12</sub>R<sub>13</sub>;

n is 0-4;

73

where R12 and R13 are independently selected from H, C<sub>1-4</sub> alkyl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR14; and R14 is selected from H, C<sub>1-4</sub> alkyl.

- 5 2. A compound according to claim 1 wherein the compound of formula I is a compound of formula II:

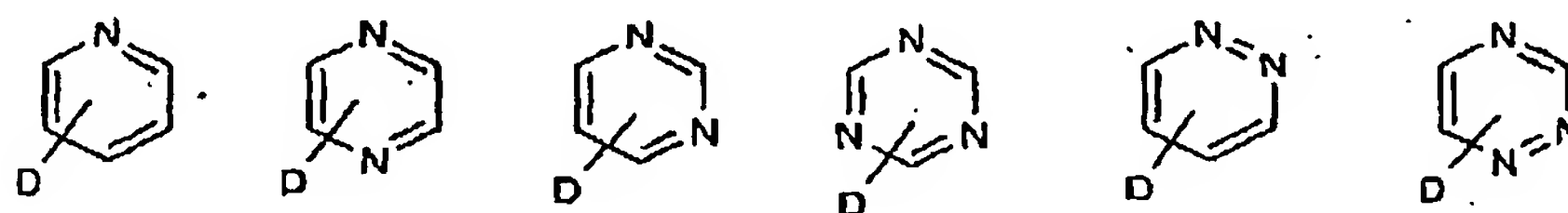


II

- 10 or pharmaceutically acceptable prodrugs, salts, hydrates, solvates, crystal forms or diastereomers thereof, wherein:

X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub>, X<sub>4</sub> are each carbon where one is substituted with Z and the rest independently with Y; or one of X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub>, X<sub>4</sub> is N, and the others are carbon where one carbon is substituted with Z and the rest independently with Y;

A is a ring selected from:



15

where D is selected from H, C<sub>1-4</sub> alkyl, halogen, amino;

Q is a bond, halogen, C<sub>1-4</sub> alkyl, O, S, SO, SO<sub>2</sub>, CO, CS;

W is:

- 20 (ii) NR1R2 where R1 and R2 are independently H, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylCF<sub>3</sub>, aryl, hetaryl, C<sub>1-4</sub> alkylaryl, C<sub>1-4</sub> alkylhetaryl, C<sub>3-8</sub> cycloalkyl, C<sub>2-6</sub> alkenyl, cyclohetalkyl, C<sub>1-4</sub> alkylcycloalkyl, C<sub>1-4</sub> alkyl cyclohetalkyl, or R1 and R2 are joined to form an optionally substituted 3-8 membered ring optionally

74

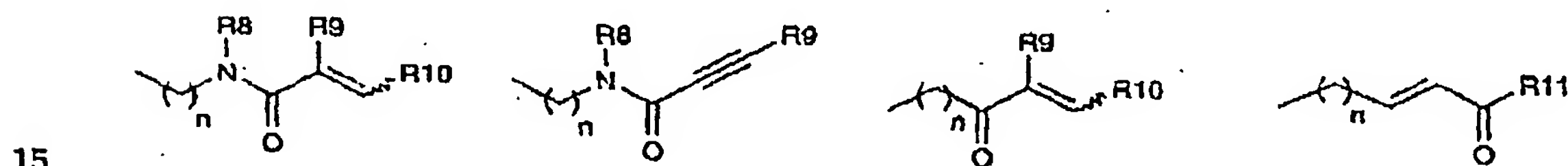
containing an atom selected from O, S, NR3; and R3 is selected from H, C<sub>1-4</sub> alkyl, aryl, hetaryl, C<sub>1-4</sub> alkyl aryl, C<sub>1-4</sub> alkyl hetaryl, COR4 where R4 is selected from H, C<sub>1-4</sub> alkyl, aryl, hetaryl;

OR

- 5 (ii) W is H, C<sub>1-4</sub> alkyl, aryl, hetaryl, C<sub>3-8</sub> cycloalkyl, cyclohetalkyl, C<sub>1-4</sub> alkylaryl, C<sub>1-4</sub> alkylhetaryl, C<sub>3-8</sub> cycloalkyl, C<sub>1-4</sub> alkylcycloalkyl, C<sub>1-4</sub> alkyl cyclohetalkyl;

Y is H, halogen, CN, CF<sub>3</sub>, nitro, OH, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylNR5R6, C<sub>1-4</sub> alkylhetaryl, OC<sub>1-4</sub> alkyl, OC<sub>2-4</sub> alkylOC<sub>1-4</sub>alkyl, OC<sub>1-4</sub> alkylNR5R6, OC<sub>1-4</sub> alkylhetaryl, OC<sub>1-4</sub> alkylcyclohetalkyl, SC<sub>1-4</sub> alkyl, SC<sub>2-4</sub> alkylOC<sub>1-4</sub>alkyl, SC<sub>1-4</sub> alkylNR5R6, NR5R6, NR5COR6, NR5SO<sub>2</sub>R6; and R5 and R6 are each independently H, C<sub>1-4</sub> alkyl, or may be joined to form an optionally substituted 3-6 membered ring optionally containing an atom selected from O, S, NR7 and R7 is selected from H, C<sub>1-4</sub> alkyl, aryl, hetaryl, C<sub>1-4</sub> alkylaryl, C<sub>1-4</sub> alkylhetaryl;

Z is selected from :



where R8 is selected from H, C<sub>1-4</sub> alkyl;

R9 and R10 are independently selected from H, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkylNR12R13, C<sub>1-4</sub> alkylOR12, C<sub>1-4</sub> alkylhetaryl or may be joined to form a 5-8 membered ring optionally containing an atom selected from O, S, SO, SO<sub>2</sub>, NR14;

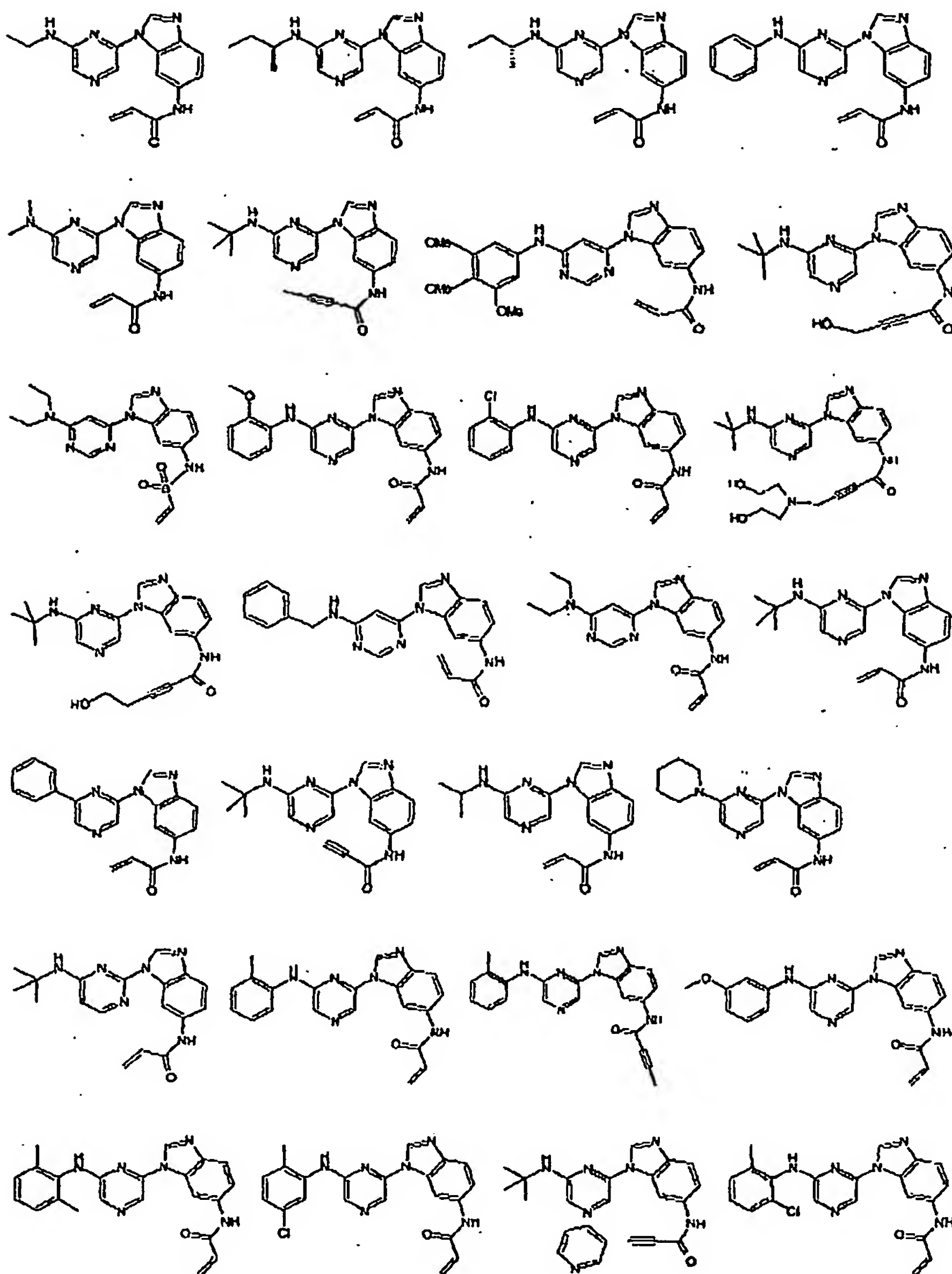
20 R11 is selected from OH, OC<sub>1-4</sub> alkyl, NR12R13;

n is 0-4;

25 where: R12 and R13 are independently selected from H, C<sub>1-4</sub> alkyl, or may be joined to form an optionally substituted 3-8 membered ring optionally containing an atom selected from O, S, NR14; and R14 is selected from H, C<sub>1-4</sub> alkyl.

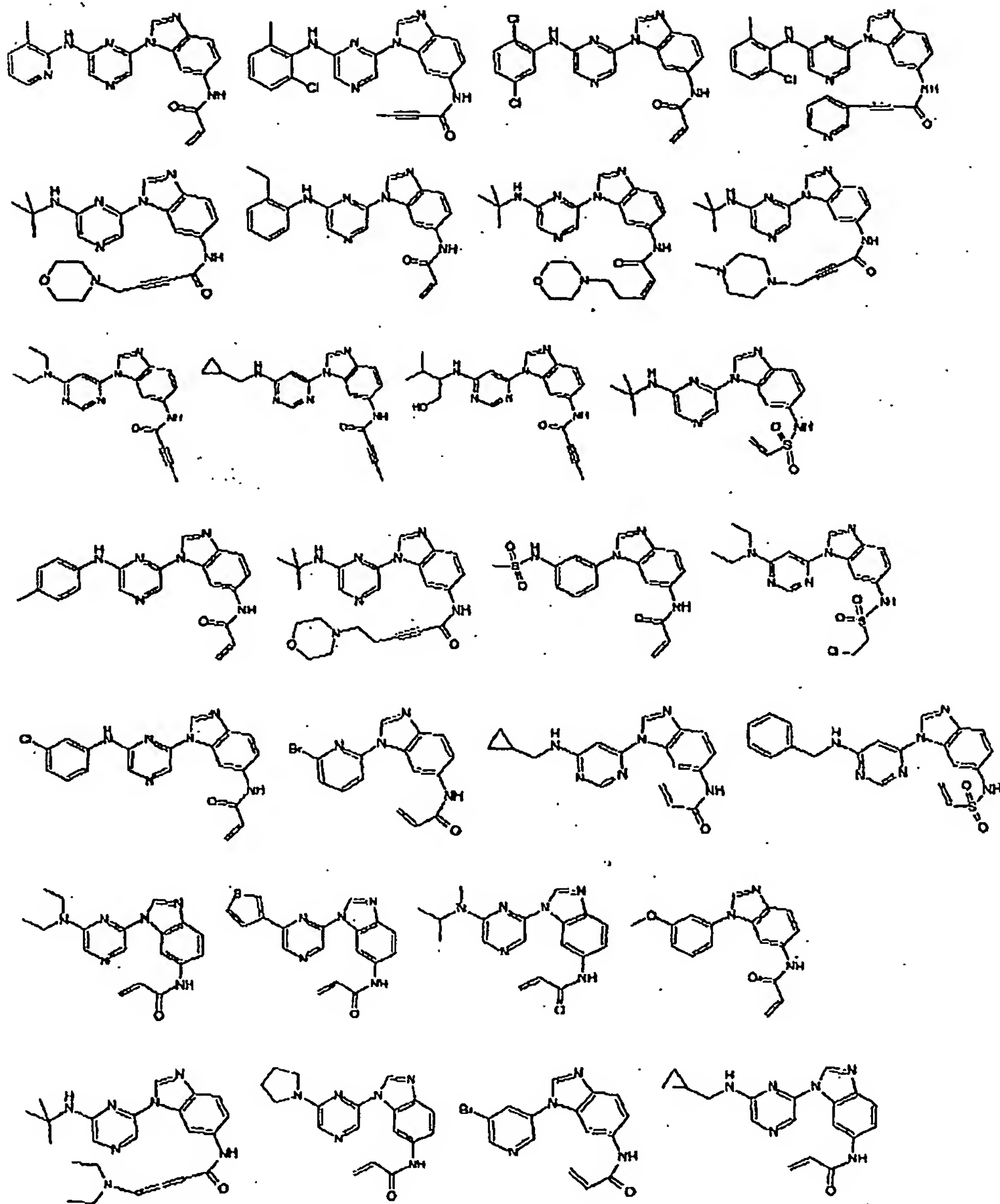
75

3. A compound according to claim 1 selected from the group consisting of:

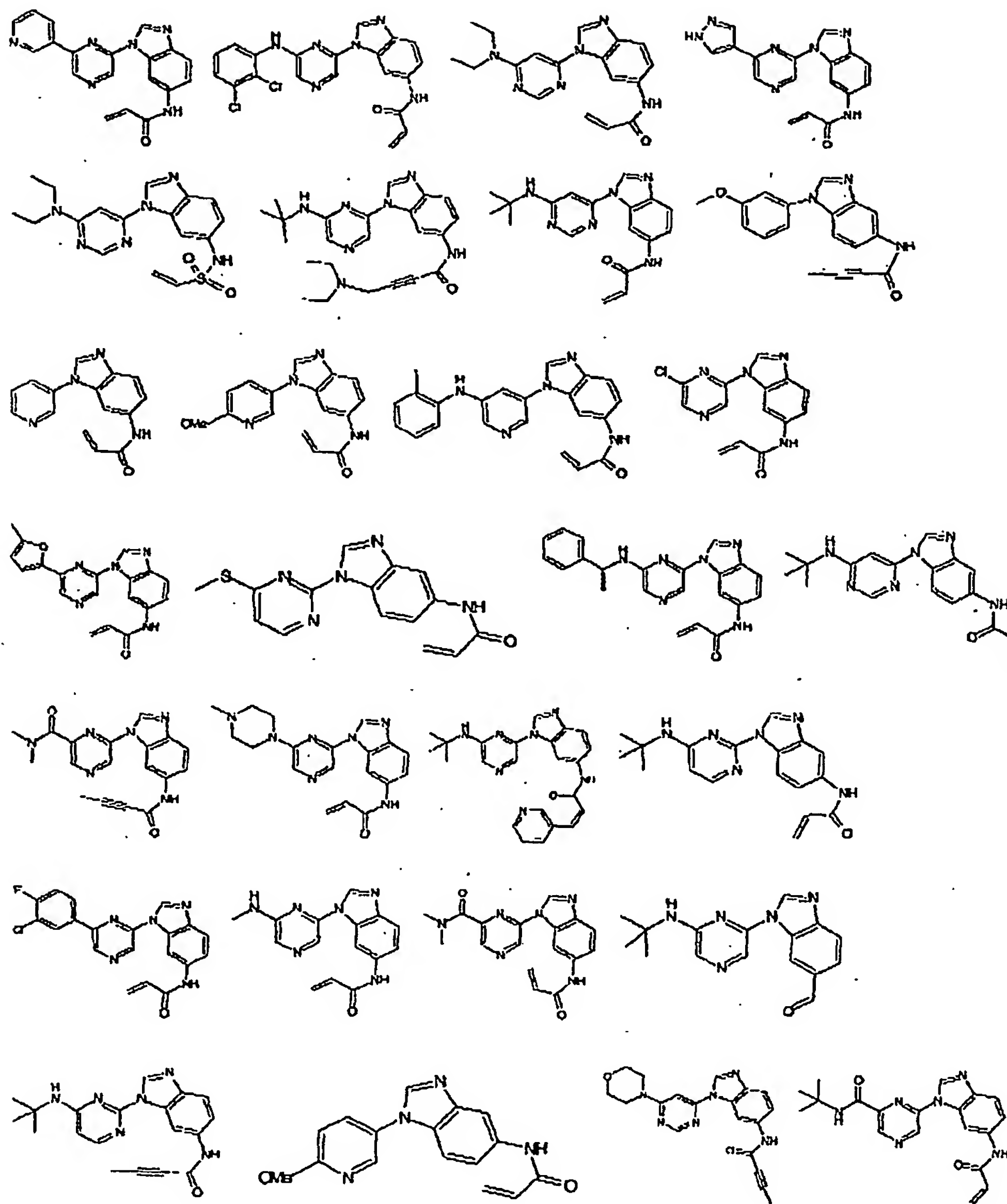


5

76

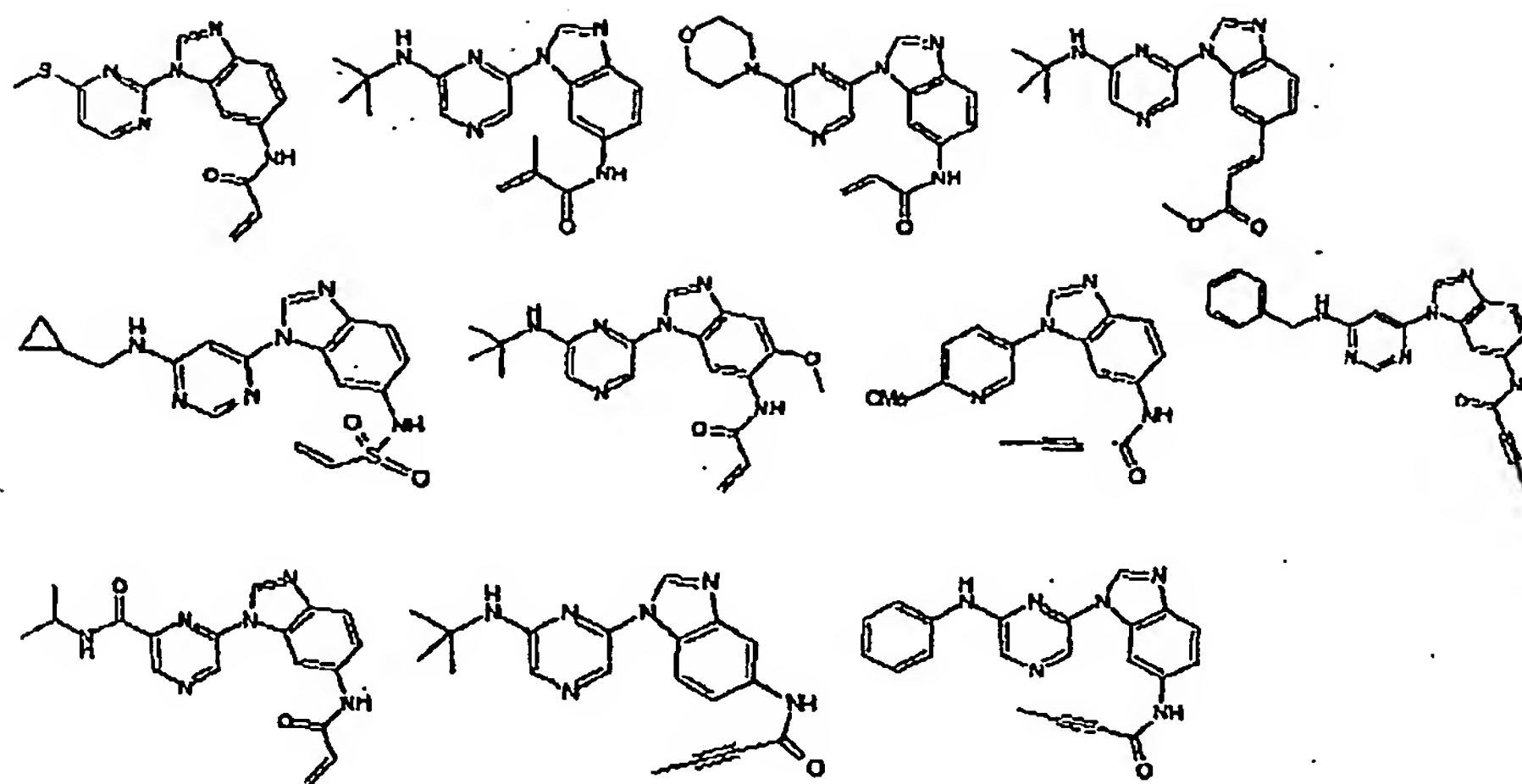


77



5

78



4. A compound according to any one of claims 1 to 3 wherein the compound irreversibly  
5 inhibits JAK-3.
5. A compound according to any one of claims 1 to 4 wherein the compound selectively  
inhibits JAK 3 with respect to JAK 1 or JAK 2.
6. A composition comprising a carrier and at least one compound according to any one  
of claims 1 to 5.
- 10 7. A method of treating a tyrosine kinase-associated disease state, the method  
comprising administering a therapeutically effective amount of at least one compound  
according to any one of claims 1 to 5 or a therapeutically effective amount of a composition  
according to claim 6.
8. Use of the compound according to any one of claims 1 to 5 or a composition according  
15 to claim 6 in the preparation of a medicament for the treatment of a JAK3-associated disease  
state.
9. A method of suppressing the immune system of a subject, the method comprising  
administering a therapeutically effective amount of at least one compound according to any  
one of claims 1 to 5 or a therapeutically effective amount of a composition according to claim  
20 6.



**AMENDED CLAIMS**

[received by the International Bureau on 17 May 2005(17.05.05);  
new claims 10-13 have been added; claims 1-9 remain unchanged (1 page)].

10. A selective JAK 3 inhibitor comprising a functionality wherein the functionality is positioned to selectively interact with the Cysteine residue close to the front lip of the ATP-binding cavity of JAK3 (CYS909) whereby the inhibitor is selective for JAK3 with respect to JAK2 and JAK1.
11. A selective JAK3 inhibitor according to claim 10 wherein the functionality irreversibly binds with the Cysteine residue.
12. A selective JAK3 inhibitor according to claim 10 or claim 11 wherein the functionality is an alkylating group.
13. A selective JAK3 inhibitor according to any one of claims 10 to 12 wherein the functionality is a Michael acceptor.